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Clinical Manifestation of Childhood Diphtheria

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Abstract

Even though diphtheria vaccination has been routinely done all around the world, some of developing country still reported outbreak. Indonesia declared diphtheria outbreak in 2017. Diphtheria is characterized by sore throat, fever and the formation of pseudo-membrane located in the tonsils, pharynx or nasal cavity. Diphtheria is very common in children. This study was conducted to determine the clinical picture of diphtheria in children at Sulianto Saroso Infectious Disease Hospital January 2018 - December 2018. The study was descriptive cross – sectional using medical records of diphtheria patients for the period January 2018 – December 2018. The sample is 141 diphtheria patients with the total sampling method. Data analysis using univariate. In this study, out of 141 children with diphtheria, the highest number of cases was recorded boy (58,2%), among 6-11years old, and fully vaccinated (60.3%). Most patient complained about sore throat (95%), fever (93.6%), and bullneck (32.6%). Majority of diphtheria patients with bilateral tonsillar membranes were also found (71.6%), followed by the majority of negative culture results (66.7%), experienced no complications (78.7%), and discharge (99.3%). Clinical characteristic that commonly appeared were sore throat, fever, and bilateral tonsillar membrane. We found it is important to diagnose and treat early to prevent complication and mortality.

Keywords: Diphtheria, Clinical Pictures, Pediatric Patients

Original Research Article

Manifestasi Klinis Difteri Anak

Abstrak

Meskipun vaksin difteri telat secara rutin dilakukan di berbagai negara, beberapa negeri berkembang masih melaporkan kejadian luar biasa (KLB). Indonesia mengumumkan KLB difteri pada tahun 2017. Difteri ditandai dengan sakit tenggorokan, demam dan terbentuknya pseudomembran yang terletak di tonsil, faring atau rongga hidung. Penyakit difteri sangat sering terjadi pada anak – anak. Penelitian ini dilakukan untuk mengetahui manifestasi klinis difteri pada anak di ruang isolasi RSPI Prof. dr. Sulianti Saroso periode Januari 2018- Desember 2018. Penelitian deskriptif *d e s a i n* cross-sectional memakai

rekam medis pasien dan dikumpulkan menggunakan metode total sampling. Analisis data secara univariat. Dalam penelitian ini dari 141 anak dengan kasus Difteri jumlah kasus tertinggi tercatat pada anak laki-laki (58,2%), berusia 6-11 tahun, diikuti status imunisasi lengkap sesuai usia (60,35). Manifestasi klinis yang paling sering ditemukan pada studi ini mencakup nyeri tenggorok (95%), demam (93,6%), dan bullneck (32,6%). Tanda klinis sebagian besar adalah membran Tonsil Bilateral (71,6%) dan mayoritas hasil kultur negatif (66,7%). Dalam studi ini, sebagian besar tidak mengalami komplikasi (78,7%) serta memiliki angka kesembuhan yang tinggi (99,3%). Pentingnya deteksi dan penanganan dini kasus sangat penting untuk mencegah komplikasi dan mortalitas.

Kata Kunci: Difteri, Gambaran Klinis, Pasien anak

INTRODUCTION

Diphtheria is an infectious disease caused by *Corynebacterium diphtheriae*. The clinical symptoms are sore throat, fever, and pseudo-membrane in the tonsil, pharynx, or nasal cavity. The microbe can produce toxins and spread them all over the body. The toxin causes irreversible inhibition of protein synthesis and epithelial cell dysfunction in the respiratory system, kidney, heart, and nervous system (Tosepu et al., 2018). Diphtheria can be easily transmitted via droplet or direct close contact with a confirmed patient (Harsanti et al., 2020). Classically, diphtheria was found in children less than 12 years. Neonates are put at higher risk due to inadequate immune systems. Thus, it was proven that completed diphtheria vaccination was able to reduce this disease incidence. It was also convinced that in the outbreak, the number of incidences correlated to local population immunity. (Hadinegoro et al., 2018).

Even though diphtheria vaccination has been routinely done all around the world, some developing countries still reported outbreaks. (Arguni et al., 2021) Thus, it is still considered a serious matter. In 2019, it was re-decreasing to 529 cases, and 23 death documented in almost all provinces of Indonesia. Hence, the case fatality rate rose to 4,35%. The next year, it was reported 259 confirmed cases and 13 deaths, while Case Fatality Rate (CFR) 5,02%. It was a significant difference from 2019 (Kemenkes RI, 2020).

Clinical symptoms of diphtheria varied from asymptomatic to life-threatening signs such as airway obstruction and myocarditis. It is common to find symptoms in oral cavity organs like the tonsil, pharynx, and larynx. Patients might come to the hospital experiencing atypical symptoms, such as dysphagia and fever. A Greyish-white pseudo-membrane appears in 1-2 days after onset, on the tonsil, and larynx, and

spread to the uvula, larynx, and trachea. Hence, clinical examination and early diagnosis are essential to avoid complications and save patients' lives. (Hadinegoro et al., 2018).

Jammer et al studied the manifestation clinic of the disease and concluded culture didn't rule out diphtheria. They also recommend giving therapy at the earliest to clinical suspects of diphtheria. (Jammer et al., 2021). This study aimed to study the clinical description of diphtheria in children at Sulianti Saroso Infectious Disease Hospital. We analyzed demography characteristics including age, gender, vaccination history, clinical symptom, and sign including the location of pseudo-membrane, diphtheria culture examination, complication, and output so that we could identify and manage holistic treatment in the future.

MATERIAL AND METHODS

This study was an observational study with a cross-sectional design conducted. We collected samples by total sampling method in 0-16 years old, inpatient children diagnosed diphtheria by pediatrician at Sulianto Saroso Infectious Disease Hospital in January-December 2018. Inclusion criteria were 0-16 years old children and diagnosed diphtheria by pediatrician. Exclusion criteria were incomplete data and patients who had diagnosed myocarditis and congenital heart disease previously. Source of secondary data was taken from medical record. We used total sampling. We collected demographic characteristic, symptom and sign and laboratory result. Analysis was done using IBM SPSS Statistics 23.0. Univariate data analysis was done by serving frequency distribution. This study was approved by ethical committee of Sulianto Saroso Infectious Disease Hospital no 39/XXXVIII.10/XI/2021.

RESULTS

Table 1. Demography Characteristic and Clinical Description

Variable	Total (n=141)
Age	
0-5 years old	60 (42,6%)
6-11 years old	62 (44%)
12-16 years old	19 (13,5%)

Variable	Total (n=141)
Gender	
Male	82 (58,2%)
Female	59 (41,8%)
Vaccination Status	
Completed	85 (60,3%)
Incomplete	39 (27,7%)
Not vaccinated	14 (9,9%)
No data	3 (2,1%)
Fever	
Yes	132(93,6%)
No	12 (6,4%)
Sore Throat	
Yes	134 (95%)
No	10 (15%)
Hoarseness	
Yes	3 (2,1%)
No	141 (97,9%)
Stridor	
Yes	23 (16,3%)
No	121(83,7%)
Bullneck	
Yes	46 (32,6%)
No	98 (67,4%)
Location of Pseudo-membrane	
Unilateral Tonsil	33 (23,4%)
Bilateral Tonsil	101 (71,6%)
Pharynx	3 (2,1%)
Larynx	1 (0,7%)
Eyes	3 (2,1%)
Culture Result	
Positive	47 (33,3%)
Negative	94 (66,7%)
Complication	
Myocarditis	26 (18,4%)
Airway obstruction	4 (2,8%)
No complication	111 (78,7%)
Outcome	
Death	1 (0,7%)
Resolution	140(99,3%)

Out of 141 children administered to Suliarto Saroso Infectious Disease Hospital were mainly 44% 6-11 years old), 58,2% boy and 60,3% had completed diphtheria vaccination. We found 93,6% of patients experienced fever, 95% patients got sore throat, 16,3% patients had stridor, and 32,6% patients had *bullneck*.

It was described in the table that pseudo-membrane in bilateral tonsil was mostly found in our study. Positive culture of *Corynebacterium diphtheria* was proven in 47 children (33,3%) while the rests weren't confirm by the examination. Complication in the study were myocarditis (18,4%) and airway

obstruction (78,7%). Almost all children had resolution (99,3%) while 1 child (0,7%) died.

DISCUSSION

We collected 141 inpatient children due to diphtheriae at National Center Sulianti Saroso Hospital. Most of the patients were 6-11 years old (n=62 people; 44,0%) and followed by 0-5 years old (n=60 people; 42,6%). This finding was in line to (Harsanti et al., 2020) that stated 5-9 years old children was the most vulnerable group to diphtheria. (Harwalkar & Kadegaon, 2019) also reported the highest distribution fell onto 6-10 years old children. Number of boys were more

than girls in our study. This finding was in line to result of (Arifin & Prasasti, 2017)'s research that pointed boys were more prone to get infected due to their outdoor activity that lead to bigger exposure to the disease. It was also supported by two other studies, (Arya et al., 2022) and (Harsanti et al., 2020). They also observed boys were in higher risk to the infection than girls. Related to this fact, Fischinger et al studied that in general, female induces adaptive humoral and cellular immune response than male. This includes higher antibody level response in the event of viral infection and vaccination. (Fischinger et al., 2019).

Role of vaccine in infection prevention is clear. In diphtheria cases, vaccination is effective to avert severe infection and even mortality. In contradict, it only has a slight influence to prevent mild infection and asymptomatic carrier infection (Kolybo, 2013). Toxoid diphtheria vaccine gives protection up to 90% to clinical diphtheria and 50-80% to the disease complication such as myocarditis, neurological deficit and mortality (Quick et al., 2000). According to (Harsanti et al., 2020), it might be correlated to low antibody titer due to inadequate booster vaccine. Interaction to schoolmates and teacher also increase possibility to *Corynebacterium diphtheriae* exposure. In order to decrease mortality in diphtheria in children, Minister of Health suggested mandatory DPT vaccine. We observed that children who had completed their vaccination were more prone to get infected than children who were unvaccinated or partially vaccinated. In agreement to our results, (Alfiansyah, 2015) and (Nawing et al., 2019) reported children with completed vaccination had the highest incident of diphtheriae. These studies also observed more children with completed vaccination experienced the disease (Arifin & Prasasti, 2017). A number of factor might causes lower effectivity of the vaccine such as patient's condition, logistic factor and epidemiologic factor (Harsanti et al., 2020). This finding reminded us the importance to check vaccine qualities which should be done by surveillance officer (Alfiansyah, 2015).

The most experienced clinical symptoms were sore throat, fever, bullneck, stridor and hoarseness. This study was in line with a research done by (Liansyah et al., 2020) which reported sore throat was the most common finding, followed by fever, stridor, hoarseness and

bullneck. A study by (Arya et al., 2022) described all diphtheria cases in children experienced sore throat and fever while bullneck and airway obstruction were less common. (Nawing et al., 2019) found most common symptoms were fever, sore throat and dysphagia. In diphtheria, fever is not usually high so that patient doesn't usually complaint about it.

We found pseudo-membrane were more frequent to be found in bilateral tonsil than unilateral tonsil. Two cases had pseudo-membrane in pharynx and eyes and one case in larynx. (Liansyah et al., 2020) also reported bilateral tonsil was more common place to seek for pseudo-membrane rather than any other locations. They described 44,6% children with diphtheriae experienced pseudo-membrane in bilateral tonsil, 32,7% in unilateral tonsil and 22,8% in pharynx.

In order to make diagnoses, clinician depends on clinical signs more than lab results. Our study shows negative culture was easier to find than positive result. (Liansyah et al., 2020) met the same conclusion. However, Early diagnosis based on clinical symptoms should be made to prevent life-threatening complication. (Dyah Nugroho et al., 2019). Sampling technique, choosing transport media, saving and delivering technique alter the result of culture examination of *C. diphtheriae* (Dyah Nugroho et al., 2019). Children met difficulties to open mouth optimally due to lymphadenopathy and bullneck or oedema. (Meera & Rajarao, 2014). Sampling technique, dry material swab or false technique in performing culture affected culture result. Thus, healthcare workers should be more careful and thorough while performing this examination. Other diseases have similarity to diphtheria are exudative tonsilitis and severe streptococcal sore throat. (Jammam et al., 2021) Twenty-six (18,4%) children in this study experienced myocarditis and four children got airway obstruction. Similar results stated myocarditis was the most common complications done by (Arya et al., 2022; Dyah Nugroho et al., 2019; Liansyah et al., 2020; Nawing et al., 2019). Sign of myocarditis wasn't met clinically. Electrocardiography and elevated aspartate transaminase were used to detect myocarditis. (Harwalkar & Kadegaon, 2019) study showed cardiac conduction disorder without myocarditis was often met in diphtheria such as asymptomatic bradycardia. Early detection to

the disorder should be done by performing vital sign examination (heart rate, blood pressure) and regularly electrocardiography.

In our study, most of the patient recovered from the disease while one patient (0,7%) passed away. This actually showed a bonam prognosis for this disease. In line to (Nawing et al., 2019) study which also proved domination of resolution as output of most patient. Mortality in children with diphtheria was associated to nutrition. Children with impaired nutritional status would experience immune deficiency so that response to vaccination wouldn't be optimal (Nawing et al., 2019). Therefore, simultaneously nutritional status improvement and completed vaccination were ways to prevent mortality. Other than that, early detection to myocarditis and early treatment with Anti Diphtheriae Serum (ADS) were also important. Completed vaccination and early treatment with ADS were proven more effective to prevent complication than unvaccinated, late ADS treatment, and inadequate number of ADS (Arya et al., 2022).

CONCLUSION

We found most diphtheria cases in 6-11 years old children, boy, and had completed basic vaccination. According to clinical symptom, greater number of our patient experienced sore throat and fever. We also found pseudo-membrane and negative culture result dominated our study. We didn't meet any complication and most of our participant resolute. By this study, we learned early detection and early treatment to diphtheria is essential to prevent complication and morbidity.

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